REMARKS

Entry of the above amendments and reconsideration of this application as amended are requested. Upon entry of the amendments, this application will contain claims 43-47, 49, 52-56, 58-60, 62-64, 68 and 73-74 pending and under consideration. The amendments are supported, for example, in passages from the application quoted below, and the amendments and following remarks are believed to address and remove all rejections of record. Therefore, allowance of this application is solicited.

Claims 43-47, 49, 52-56, 68 and 73 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. As one basis for this rejection, the Office Action cites the use of "consisting essentially of" in these claims. This transition is well known and has long been used in US patent practice. However, to remove the issue from the present prosecution, this phrase has been changed to "comprising". As another basis for rejection, the Office Action cited the use of "at least about" in claim 56. Again, to remove the issue from the present prosecution, this phrase has been removed in favor of "greater than about". In view of these changes, withdrawal of this rejection is solicited.

Claims 43, 45-47, 52, 60, 68 and 73-74 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chu et al. (U.S. 4,888,366), as evidenced by McKay, W. (U.S. 5,972,368). To the extent maintained, this rejection is traversed for the following reasons.

Claims 43, 60, 73 and 74, the independent claims, have each been amended so as to be directed to osteogenic compositions "effective for the induction of new bone growth in a human patient", wherein the compositions require:

an osteogenic factor effective to stimulate both osteoblasts and osteoclasts when administered to a human, and wherein said osteogenic factor is incorporated into said sponge implant device in such an amount as to stimulate the osteoclasts sufficiently to cause an increase in the rate of resorption of said resorbable sponge matrix when said sponge implant device is implanted in a human; and

wherein said particulate biocompatible mineral is resorbed more slowly than said resorbable sponge matrix when said sponge implant device is implanted in a human and thereby provides a scaffold for bone ingrowth that remains after said resorbable sponge matrix is resorbed.

As is disclosed in the application at page 5, lines 9-23:

> A particular feature of the present invention relates to the discovery that the inclusion of an osteogenic factor, especially an osteoblast- and osteoclast-stimulating osteogenic factor, in a resorbable sponge composition causes a substantially accelerated resorption of the sponge. This rapid resorption can diminish or eliminate the capacity of the sponge composition to effectively stimulate and support new bone formation in a void filled with the sponge composition. This is particularly the case in primates, including humans, in which the rate of new bone formation is relatively slow.

Further, page 8, lines 4-15 of the application describe that:

> Accordingly, a feature of the present invention is the provision of an osteogenic composition in the form of a sponge that includes a substantial amount of a relatively slowly-resorbed mineral component that remains at the implant site after the carrier has been rapidly resorbed, in order to provide a scaffold for new bone formation that is not prematurely resorbed due to the osteoclastic potentiation by the bone morphogenic protein in the composition.

Turning now to a detailed discussion of the pending rejection, when rejecting claims under 35 U.S.C. § 103, "the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art." *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783 (Fed. Cir. 1992). To establish a prima facie case of obviousness, the Examiner must provide objective evidence 1) of some suggestion or motivation to combine or modify one or more prior art references, 2) that the suggested combination or modification has a reasonable expectation of success, and 3) that the prior art reference or references, when combined, suggest or teach all of applicant's claim

limitations. MPEP § 2143. As held by the Federal Circuit, "[t]hese findings or evidence must be specific, clear, and particular." *In re Lee*, 61 U.S.P.Q. 2d 1430, 1433-34 (Fed. Cir. 2002). "Broad conclusory statements regarding the teaching of multiple references, standing alone, are not [considered sufficient] 'evidence' " to support a finding of prima facie obviousness. *In re Dembiczak*, 50 U.S.P.Q. 2d 1614, 1617 (Fed. Cir. 1999); See also, *Ex Parte Levengood*, 28 U.S.P.Q. 2d 1300, 1301 (Bd. Pat. App. & Int. 1993).

Obviousness determinations must be performed without "entry into the 'tempting but forbidden zone of hindsight.'" *Dembiczak*, 50 U.S.P.Q. 2d at 1616 (Fed. Cir. 1999). More specifically, in *Dembiczak*, the Federal Circuit offered the following guidance:

> [m]easuring a claimed invention against the standard established by section 103 requires the oft-difficult but critical step of casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. . . .

Dembiczak, 50 U.S.P.A. 2d at 1617. The best protection against the use of hindsight is a rigorous application of the motivation criterion, which results in most *prima facie* obviousness determinations hinging on an objective finding of some motivation or suggestion to combine or modify one or more prior art references. See, *Dembiczak*, 50 U.S.P.Q. 2d at 1617; *In re Roufett*, 47 U.S.P.Q. 2d 1453, 1457-58 (Fed. Cir. 1998).

It is likewise important to note in this context that in determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983) "[A] patentable invention may lie in the discovery of the source of a problem even though the

remedy may be obvious once the source of the problem is identified. This is part of the 'subject matter as a whole' which should always be considered in determining the obviousness of an invention under 35 U.S.C. § 103." *In re Sponnoble*, 405 F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969).

When considered in a proper analysis under 35 U.S.C. § 103, it is submitted that the present claims are nonobvious and therefore patentable in relation to the applied references. As disclosed in the present application, including the above-quoted passages, one feature of the invention involves the discovery that the inclusion of an osteoblast- and osteoclast-stimulating osteogenic factor in a composition including a resorbable carrier matrix causes a rapid and premature resorption of the carrier matrix. This rapid resorption of the carrier can diminish or eliminate the capacity of the composition to effectively stimulate and support new bone formation in a void filled with the composition. This particularly true in the case of humans, in which the rate of new bone formation is relatively slow.

Accordingly, the compositions presently claimed are effective to induce new bone growth in humans and include a high proportion of a long-lasting particulate mineral material that remains after the sponge matrix material is resorbed, along with the osteoclast- and osteoblast-stimulating osteogenic factor present in an amount that stimulates a rapid osteoclastic removal of the sponge matrix material. The Chu et al. reference does not disclose the problem discovered by applicant, or how to overcome it. Only the applicant's discovery disclosed in the application points up this need; however, use of applicant's own specification in filling in the gaps left by the prior art would be an inappropriate use of hindsight in making the obviousness rejection.

Additionally, the independent claims are directed to osteogenic sponge compositions that comprise a "three-dimensionally stable but flexible" device. The Chu et al. reference fails to

motivate one of ordinary skill in the art to carry out this claimed feature and in fact teaches the skilled artisan away from this feature -- to prepare a rigid device. As evidence of this teaching away, the following passages of Chu et al. are offered.

1. At column 2, lines 19-20, Chu et al. describes the shortcomings of the prior art, stating that "[n]one of the foregoing compositions result in a homogenous, rigid preparation which can be used directly for implantation in bone...".

2. At column 2, lines 36+, Chu et al. describes how its compositions are prepared (including drying at ambient pressures and slightly elevated temperatures), concluding at lines 47-51 with the teaching that "[w]hen the preparation process is conducted in this way, the resulting compositions are characterized as being rigid with a compression strength of at least 20 Newtons per square centimeter...".

3. At column 9, lines 24-26, Chu et al. teaches that "[d]rying by lyophilization at the final step produces a spongy product nonconforming with regard to strength and homogeneity."

4. In Example 2, Chu et al. prepare a lyophilized composition (not of the Chu et al. invention) as a comparative example, and note its relatively poorer performance in Example 5.

With regard to the rejected claims requiring lyophilized collagen, it is also relevant to note that the Chu et al. reference teaches that lyophilization processing, as opposed to the Chu et al. "controlled drying" processes, leads to a preparation having different physical properties. Accordingly, the assertions in the Office Action that the materials must be inherently the same because the ingredients are the same, is established as incorrect in the teachings of the Chu et al. reference itself. In this regard, it is well established in the law that a proper rejection under 35 USC 103 cannot selectively rely upon certain aspects of a reference while ignoring other aspects that teach away. It is respectfully submitted that the reasoning for the rejection given in the

Office Action inappropriately disregards the above-noted teachings away of the Chu et al. reference concerning the dependence of the properties of the formed material upon the manner in which it is prepared, without explaining how or why they can be discounted in making the rejection. In addition, it is noted that the McKay reference is not relied upon as filling the above-noted deficiencies of the Chu et al. reference, nor could it properly be relied upon for this purpose.

In summary, in view of the foregoing discussions, it is submitted that claims 43, 45-47, 52, 60, 68 and 73-74 require combinations of features that are not obvious over Chu et al. as evidence by McKay. Withdrawal of the rejections of these claims is therefore solicited.

Claims 43-44 and 56-59 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chu et al. (U.S. 4,888,366), as applied to claim 43, in view of Geistlich et al. (U.S. 5,573,771). To the extent maintained or applied to any of the claims as amended, this rejection is also traversed. The deficiencies of the primary Chu et al. reference in teaching or suggesting the combinations required by the rejected claims are detailed in the discussions above. Geistlich et al. is relied upon in the Office Action only for its teaching of the use of bone particles as the particulate biocompatible mineral, and has not and could not properly be relied upon to teach the noted deficiencies of Chu et al. Withdrawal of this rejection is therefore solicited.

Claims 43, 52-55, 60 and 62-64 and 56-59 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chu et al. as applied to claims 43 and 52, in view of McKay. To the extent maintained or applied to any of the claims as amended, this rejection is also traversed. The deficiencies of the primary Chu et al. reference in teaching or suggesting the combinations required by the rejected claims are detailed in the discussions above. McKay is relied upon in the Office Action only for its teaching of the use of BMP-2, and has not and could not properly

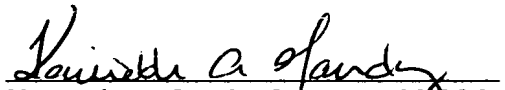
be relied upon to teach the noted deficiencies of Chu et al. Withdrawal of this rejection is therefore solicited.

Claims 43 and 49 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Chu et al., as applied to claim 43, in view of Michelson (U.S. 5,785,710).). To the extent maintained or applied to any of the claims as amended, this rejection is also traversed. The deficiencies of the primary Chu et al. reference in teaching or suggesting the combinations required by the rejected claims are detailed in the discussions above. Michelson is relied upon in the Office Action only for its teaching of a spinal implant fusion cage, and has not and could not properly be relied upon to teach the noted deficiencies of Chu et al. Withdrawal of this rejection is therefore solicited.

In conclusion, in view of the foregoing amendments and remarks, it is believed that all rejections have been overcome and that this application is in condition for allowance containing claims 43-47, 49, 52-56, 58-60, 62-64, 68, and 73-74. Prompt action to that end is respectfully solicited.

If the Examiner believes that any rejection or objection remains applicable to this application, the Examiner is requested to telephone the undersigned attorney to afford an opportunity for an interview of the case to address the issues.

Respectfully submitted,



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